REMARKS

Claims 54, 57-60, 66, 68-77, 79-84, and 86-90 were pending in the application. Claims 54, 60, 68-71, 76, 77, 79-81, 83-84, 86-87, 89-90 have been amended. New claims 91-113 have been added. Following entry of this Amendment and Response, claims 54, 57-60, 66, 68-77, 79-84 and 86-113 will be pending.

Support for new claims 91-113 can be found throughout the specification and in the claims as originally filed. Support for the amendment to claims 54, 60, 68-71, 76, 77, 79-81, 83-84, 86-87, 89-90 and new claims 91-145 can be found in the claims as originally filed and throughout the specification. Specifically, support for amended claims 69-70, 76-77, 83-84 and new claims 91-113 is available, at least, for example, at page 37, line 1 through page 38, line 38. Support for amended claims 79-80, 86-87, 89-90 and new claims 91-113 is available, at least, for example, at page 33, line 28 through page 36, line 14. Support for amended claim 68 and new claims 91-113 is available, at least, for example, at page 36 (lines 23-25).

Since the claim amendments and new claims made herein merely incorporate subject matter previously claimed and examined in the present application in the currently pending claims, no additional search is required and no new issues of patentability have been raised. Therefore, the claim amendments and new claims made herein are permissible under 37 C.F.R. §1.116, and Applicant respectfully requests that the present Amendment and Response be entered.

No new matter has been added. The foregoing claim amendments should in no way be construed as an acquiescence to any of the Examiner's rejections, and have been made solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Information Disclosure Statement

Applicant gratefully acknowledges the Examiner's indication that the IDS and accompanying PTO/SB/08 Form submitted on December 15, 2006 have been considered.

Acknowledgment of the Examiner's Withdrawal of Certain Rejections and Objections

Applicant gratefully acknowledges the Examiner's indication that "[a]ny objection or rejection of record which is not expressly repeated in this action has been overcome by

Applicant's response or by further consideration and withdrawn." In this regard, Applicant notes that the following rejections and objections have been withdrawn: (a) the previous objection to the specification as containing an incomplete priority statement; (b) the previous rejection of claim 66 under 35 U.S.C. 112, first paragraph for lacking a fully enabling disclosure; (c) the previous rejection of claims 81-84 and 86-87 under 35 U.S.C 112, second paragraph as being indefinite; and (d) the provisional rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 as being obvious over claims 55-62 and 64 of co-pending U.S.S.N. 10/003,211.

Obviousness-Type Double Patenting

Claims 54, 57-60, 66, 68-77, 79-84 and 86-90 are rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-16 of U.S. Patent No. 5,925,351, claims 1-14 of U.S. Patent No. 6,403,087 and claims 1-11 of U.S. Patent No. 6,669,941. *Applicant respectfully disagrees and traverses this rejection on the grounds that the USPTO has consistently recognized the subject matter of the instant application as patentably distinct under 35 USC § 121 from the subject matter of the cited claims in US Patent No. 6,403,087 (from which the instant application is a divisional) and US Patent Nos. 5,925,351, and 6,669,941.*

With respect to US Patent No. 6,403,087, Applicant submits that the instant application was filed as a divisional application claiming priority to US Patent No. 6,403,087. Therefore, the subject matter of the instant application has been identified as being patentably distinct from the invention of US Patent No. 6,403,087 in accordance with 35 USC § 121. Thus, an obviousness-type double patenting rejection in view of the parent in which the restriction was issued is improper.

With respect to US Patent Nos. 5,925,351, and 6,669,941, Applicant submits that the restrictions issued in these related applications were similar to the restriction of the claims in US Patent No. 6,403,087. Based on the similarity of the restrictions and the groups cited therein, the the claimed methods of inhibiting LT-βR signaling have been recognized by the USPTO as being patentably distinct from claims 1-16 of U.S. Patent No. 5,925,351 and claims 1-11 of U.S. Patent No. 6,669,941. The following table details the restriction requirements issued during prosecution of US Patent Nos. 5,925,351; 6,403,087; and 6,669,941.

	US Patent No. 5,925,351	US Patent No. 6,403,087*	US Patent No. 6,669,941
Restriction requirement issued during prosecution and Applicant's election	***Election: Group I***	***Election: Group II***	***Election: Group I***
	Group I (claims 1-14 and 38-49) drawn to a method of treating immunological disease by administration of a LT-βR blocking agent selected from the group consisting of a soluble lymphotoxin-B receptor, and antibody against LT-B receptor, and an antibody against surface LT ligand, including monoclonal antibodies and Fc domains, and wherein claims 38-49 are drawn to a therapeutically effective composition having components identical to those described herein;	***Group I*** (claims 1-14 and 38-53) drawn to a method of treating or reducing the effects, severity or advancement of an immunological disease by administering an LT-βR blocking agent, a composition comprising an LT-βR blocking agent and a method for selecting an LT-βR blocking agent;	***Group I***: Claims 1-14, 38-49, drawn to a method of treating immunological diseases by administering a LTBR blocking agent, and to compositions comprising a LTBR blocking agent;
	Group II (claims 15-37) drawn to an in vivo method of inhibiting Th1 cell-mediated immune response by administration of a LT-βR blocking agent selected from the group consisting of a soluble lymphotoxin- β receptor, and antibody against LT-β receptor, and an antibody against surface LT ligand, including monoclonal antibodies and Fc domains, and further including a method wherein the response to treatment is cellular or organ rejection, or autoimmune disease;	***Group II*** (claims 15-37) drawn to a method of inhibiting Th1 responses by administering an LT-βR blocking agent;	***Group II:*** Claims 15-37, drawn to an in vivo method of inhibiting Th1 cell-mediated immunity by administering a LTBR blocking agent;
	Group III (claims 50-53) drawn to an in vitro method of selecting a LT-βR blocking agent, wherein tumor cells are cultured in the presence of an activating agent and anti-tumor activity is determined, including the use of a lymphotoxin α/β heterodimer or an antibody as activating agent; and	***Group III*** (claims 54-67) drawn to a method for inhibiting signaling through LT-βR; and	***Group III***: Claims 50-53, drawn to a method for selecting an LTBR blocking agent;
	Group IV (claims 54-67) drawn to an in vivo method of inhibiting LT-βR signaling without inhibiting TNF-R signaling, by administration of a LT-βR blocking agent selected from the group consisting of soluble lymphotoxin-B receptor, and antibody against LT-β receptor, and an antibody against surface LT ligand, including monoclonal antibodies and Fc domains.	***Group IV*** (claims 68-69) drawn to a method for treating IB syndrome by administering an LT-βR fusion protein. ** Instant appln. claims priority to 6,403,087 patent; filed as a divisional to Group III claims*	***Group IV:*** Claims 54-67, drawn to an in vivo method for inhibiting signalling through LTBR; and ***Group V:*** Claim 50, drawn to a method for detecting C antigen.

Rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-14 of U.S. Patent No. 6,403,087

Applicant respectfully submits that the rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-14 of U.S. Patent No. 6,403,087 (hereinafter the " '087 patent") is improper.

The instant application was filed as a divisional application claiming priority to the '087 patent, and was filed based on the claim restriction issued during prosecution of the '087 patent. The original claims of the '087 patent were drawn to four different inventions, as indicated in the above table, as well as in the enclosed copy of the office action issued during prosecution of the '087 patent (enclosed herewith as Appendix A).

In response to the restriction requirement issued during prosecution of the '087 patent, Applicant chose Group II, *i.e.*, claims drawn to a method inhibiting Th1 immune responses.

The instant application was subsequently filed as a divisional application claiming priority to the '087 patent and directed to the Group III invention, i.e., a method for inhibiting signaling through LT-βR. As such, Applicant submits that claims 54, 57-60, 66, 68-77, 79-84 and 86-90 of the instant application are patentably distinct from claims 1-14 of the '087 patent as established under 35 USC § 121.

In view of the above, reconsideration and withdrawal of the obviousness-type double patenting rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 in view of claims 1-14 of U.S. Patent No. 6,403,087 is respectfully requested.

Rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-16 of U.S. Patent No. 5,925,351

Applicant respectfully submits that the rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-16 of U.S. Patent No. 5,925,351 is improper.

During prosecution of U.S. Patent No. 5,925,351 (hereinafter the '351 patent), restriction of the claims was required by the Examiner to the four inventions described in the above table (a copy of the restriction requirement is also enclosed as Appendix B). In response, Applicant

elected the Group I invention with traverse. Upon reconsideration, the Examiner maintained the restriction.

Applicant submits that elected Group I of the '351 patent, *i.e.*, a method of treating immunological disease by administration of a LT-βR blocking agent, was identified as being patentably distinct from the subject matter of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 in the instant application. Moreover, the claims in the '351 and the '087 patent were similarly restricted during prosecution, *i.e.*, methods of inhibiting LTBR signaling (see Groups III and IV in the '087 and '351 restriction requirements, respectively) were identified as being patentably distinct from the elected invention in each patent. Thus, in keeping with the position of the USPTO, Applicant submits that claims 1-16 of the '351 patent directed to the Group I invention, *i.e.*, method of treating an immunological disease, are patentably distinct from the claims in the instant application, directed to methods for inhibiting LT-βR signaling.

In view of the above, reconsideration and withdrawal of the obviousness-type double patenting rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 in view of claims 1-16 of U.S. Patent No. 5,925,351 is respectfully requested.

Rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-11 of U.S. Patent No. 6,669,941

Applicant respectfully submits that the rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-11 of U.S. Patent No. 6,669,941 is improper.

During prosecution of U.S. Patent No. 6,669,941 (hereinafter the '941 patent), the claims were restricted according to the five groups described in the above table (a copy of the restriction requirement issued in the '941 patent is enclosed herewith as Appendix C). In response, Applicant elected the Group I invention, *i.e.*, a method of treating an immunological disease.

Applicant submits that the restriction requirement issued during prosecution of the '941 patent was consistent with the restriction of the claims in the '087 patent, *i.e.*, methods of treatment (see Groups I in both the '087 and '941 restriction requirements) were identified as patentably distinct from methods of inhibiting LTBR signaling (see Groups III and IV in the '087 and '941 restriction requirements, respectively). In keeping with the position of the

USPTO, Applicant submits that claims 1-11 of the '941 patent are patentably distinct from the claims in the instant application, directed to methods for inhibiting LT-βR signaling. As such, Applicant respectfully requests reconsideration and withdrawal of the obviousness-type double patenting rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 in view of claims 1-11 of U.S. Patent No. 6,669,941.

In view of the above, Applicant respectfully requests that the rejection of claims 54, 57-60, 66, 68-77, 79-84 and 86-90 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-16 of U.S. Patent No. 5,925,351, claims 1-14 of U.S. Patent No. 6,403,087 and claims 1-11 of U.S. Patent No. 6,669,941 be reconsidered and withdrawn.

CONCLUSION

In view of the remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicant's Attorney could be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: September 24, 2007

Respectfully submitted,

By _____

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Patent and Trademark Office
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Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
[illegible]	[illegible]	[illegible]	[illegible]

KERRY A FLYNN
BIOGEN INC
[illegible]

EXAMINER	
[illegible]	
ART UNIT	PAPER NUMBER
[illegible]	[illegible]

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

ENTERED AR

BIOGEN, INC. - IP DEPT.
JUN 23 2000
REFERRED TO NDC
NOTED BY ph

REMINDER 03JL2000
ACTION DUE 20JL2000
END OF STAT 20DE2000

"APPENDIX A"

Office Action Summary

Application No.	Applicant(s)	
09/[illegible]	[illegible]	
Examiner	Group Art Unit	
[illegible]		

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE one MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on [illegible].

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1 – 69 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☐ Claim(s)_____ is/are rejected.

☐ Claim(s)_____ is/are objected to.

☒ Claim(s) 1 – 69 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☒ Other Post Allowance and Service

Office Action Summary

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

GroupI, claim(s)1-14, 38-53 , drawn to a method of treating or reducing the effects, severity or advancement of an immunological disease by administering an LT-βR blocking agent, a composition comprising an LT-βR blocking agent and a method for selecting an LT-βR blocking agent, classified in class 514, subclass 2.

Group II, claim(s) 15-37, drawn to a method of inhibiting Th1 responses by administering an LT-βR blocking agent, classified in class 514, subclass 2.

Group III, claim(s) 54-67, drawn to a method for inhibiting signalling through LT-βR, classified in class 514, subclass 2.

Group IV, claim(s) 68-69, drawn to a method for treating IB syndrome by administering an LT-βR fusion protein, classified in class 424, subclass 85.1.

2. The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of Group II is drawn to inhibiting Th1 responses, Group III to inhibiting signalling through LT-βR, Group IV to treatment of IB syndrome. In the instant case the different inventions are all drawn to different methods of use as in Groups II-IV. Each of these methods are drawn to different manifestations of various diseases and are associated with different etiologies and rely on different endpoints. The invention of Groups II and III differs from the other three groups in needing only to inhibit

Th1 responses and inhibiting signalling through LT-βR, and need not be exacted to achieving treatment of a disease state.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

4. The species are as follows:

a) hypersensitivity; b) transplants; c) autoimmune disorers.

5. The claims are deemed to correspond to the species listed above in the following manner: a) hypersensitivity (claims 29-32); b) transplants (claims 33-34); c) autoimmune disorers (claims 35-36);

The following claim(s) are generic: Claims 29, 33, 35.

6. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the Th1 responses sought to be inhibited contributes to the above named diseases/conditions which are etiologically different and distinct from each other, as well as independent of the presence of the others.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations

of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

7. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. **Please Note**: In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-305-3704. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Paula K. Hutzell, Ph.D., Supervisory Patent Examiner at Paula.Hutzell@uspto.gov or 703-308-4310. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

10. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-3014.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Geetha P. Bansal whose telephone number is (703) 305-3955. The examiner can normally be reached on Mondays to Thursdays from 7:00am to 4:30pm and

alternate Fridays from 7:00am to 3:30pm. A message may be left on the examiner's voice mail service.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Anthony Caputa, can be reached on (703) 308- 4995.

12. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 9, 2000

GEETHA P. BANSAL
PATENT EXAMINER

UNITED STA DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

RECEIVED
NOV 20 1996
FISH & NEAVE - PATENT DEPT.
REFERRED TO
NOTED BY

EXAMINER	
ART UNIT	PAPER NUMBER

FILE COPY

DATE MAILED:

RECEIVED
NOV 21 1996
Biogen, Inc. - IP DEPT.

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

Entered Computer

☑ This application has been examined ☐ Responsive to communication filed on ____ / ____ / ____ REFERRED TO ____ NOTED BY ____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-62 are pending in the application.
   Of the above, claims 7-31 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled
3. ☐ Claims _____ are allowed
4. ☑ Claims 1-6, 32-62 are rejected.
5. ☐ Claims _____ are objected to
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☑ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____ has been ☐ approved, ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

"APPENDIX B"

15. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

Group I. Claims 1-14, and 38-49, wherein claims 1-14 are drawn to a method of treating immunological disease by administration of a LT-β-R blocking agent selected from a group consisting of a soluble lymphotoxin-β receptor, an antibody against LT-β receptor, and an antibody against surface LT ligand, including monoclonal antibodies and Fc domains, and wherein claims 38-49 are drawn to a therapeutically effective composition having components identical to those described hereinbefore, classified in Class 424, subclasses 85.1+, 130.1+, and 520, and Class 514, subclass 2.

Group II. Claims 15-37, drawn to an in vivo method of inhibiting Th1 cell-mediated immune response by administration of a LT-β-R blocking agent selected from a group consisting of a soluble lymphotoxin-β receptor, an antibody against LT-β receptor, and an antibody against surface LT ligand, including monoclonal antibodies and Fc domains, and further including a method wherein the response to treatment is cellular or organ rejection, or autoimmune disease, classified in Class 424, subclasses 85.1, 134.1, 141.1, 143.1, 192.1, and 520, and Class 530, subclasses 351, 388.22, 387.1, and 388.1.

Group III. Claims 50-53, drawn to an in vitro method of selecting a LT-β-R blocking agent, wherein tumor cells are cultured in the presence of an activating agent and anti-tumor activity is determined, including the use of a lymphotoxin α/β heterodimer or an antibody as activating agent, classified in Class 435, subclasses 4, 7.21, and 69.1.

Group IV. Claims 54-67, drawn to an in vivo method of inhibiting LT-β-R signaling without inhibiting TNF-R signaling, by administration of a LT-β-R blocking agent selected

from a group consisting of a soluble lymphotoxin-β receptor, an antibody against LT-β receptor, and an antibody against surface LT ligand, including monoclonal antibodies and Fc domains classified in Class 424 subclasses 85.1, 134.1, 141.1, 143.1, 192.1, and 520, and Class 530, subclasses 351, 388.22, 387.1, and 388.1.

16. The inventions are distinct, each from the other because of the following reasons:

The inventions of Groups I, II, III, and IV are materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and enablement criteria. Thus, the methods comprise patentably distinct subject matter and restriction is necessary because they raise different issues regarding patentability, fields of search, and enablement.

The composition of Group I and the methods of Groups II, and IV are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the product as claimed can be used in materially different processes such as those recited in Groups II and IV.

17. Election of Species

If Group I, II, or IV is elected, then an election of species will be required. This application contains claims directed to the following patentably distinct species of lymphotoxin-β receptor blocking agents:

A. Soluble lymphotoxin-β receptor

B. an antibody against LT-β receptor

C. an antibody against surface LT ligand

The species are considered patentably distinct because they are structurally distinct proteins. Upon election of one of the foregoing groups, applicant is further required to elect one of the three disclosed species (A–C).

The invention of Group II (claim 34) further recites the following species of diseases:

D. multiple sclerosis

E. insulin-dependent diabetes

F. sympathetic ophthalmia

G. uveitis

H. psoriasis

The species are considered patentably distinct because they are diseases having different etiologies and therapeutic endpoints, which necessitate different searches and raise different enablement issues. Thus, upon election of Group II, applicant is further required under 35 U.S.C. § 121 to elect a single species (D–H) for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 15, 38, and 54 are generic.

18. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a generic claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election,

applicant must indicate which are readable upon the elected species. *MPEP* § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 of the other invention.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and/or recognized divergent subject matter, restriction for examination purposes as indicated is proper.

19. During a telephone conversation with Attorney Kerry Flynn on 9/19/96, a provisional election was made with traverse to prosecute the invention(s) of Group I, Species A. Affirmation of this election must be made by Applicant in responding to this Office action. Claims 15-37 and 50-67 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention. Within Group I, claims 7-14 and 42-49 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to non-elected species of the invention. Claims 1-6 and 38-41 are being examined.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

20. The Declaration and Power of Attorney, Copy of Notice to Comply with Sequence Requirements, Computer Readable Form (CRF) of the Sequence Listing and accompanying statements, and Preliminary Amendment filed on 10/16/95 have been entered. The Information Disclosure Statement filed on 11/27/95 has been entered and considered. The Associate Power of Attorney documents filed on 1/5/96 and 9/16/96 have been entered. The CRF filed on 9/18/96 has been entered.

21. Objections to the specification and claims

a. The brief description of Figure 6 (p. 10) is objected to because it fails to describe all 3 panels of the drawing. Amendment of the description to replace "6" with --6A-C-- , and to incorporate specific references to each of the three panels, and the addition of appropriate labels (A, B, and C) to the drawing will overcome this objection.

b. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

c. p. 27, lines 12 and 20: the ATCC accession numbers are missing.

d. The abbreviation "LT-β-R" in claims 1 and 38 should be spelled out, as it is in claims 2, 5, 6, and 39-41.

e. The abbreviation "LT" in claims 2, 5, 39 and 40 should be spelled out.

22. Rejections under 35 U.S.C. § 112

a. Claims 1-6 and 38-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

i. Claims 1-6 are drawn to a method for treating or reducing the advancement,

severity or effects of any and all immunological diseases by administering a therapeutically effective amount of any LT-β-R (lymphotoxin β receptor) blocking agent. Claims 38-41 are drawn to a pharmaceutical composition comprising a therapeutically effective amount of a lymphotoxin-β blocking agent.

Although examples of diseases having an immunologic etiology are disclosed in the specification (e.g., pp. 11-15), tne phrase "immunological disease" is not defined. The meaning of this phrase is critical to enablement, and in its broadest sense it would appear to encompass any disease involving elements of the immune system. However, the precise role of LT-β and LT-β-R-blocking agents in the etiology of the immunological diseases exemplified *supra* is not disclosed in the specification. Further, there is uncertainty in the art associated with immune-mediated responses, as related to the treatment of disease. For example, Browning et al. (1993; of record) disclose that the initiation of an immune response is a complex, multi-step and multi-component process involving both cell-contact- and soluble cytokine-mediated events. The reference further states that the roles of these mediators "are somewhat of an enigma since in vivo experiments suggest very critical functions, yet the corresponding in vitro work has not led to a very clear picture of their place in T and B cell regulation" (p. 847, paragraph 1, last sentence). In view of these uncertainties, it is unpredictable whether any "LT-β-R-blocking agent" is enabled for use in a method of treating any immunologic disease encompassed by the claimed invention.

The specification provides limited guidance with regard to how to make and use a therapeutically effective LT-β-R blocking agent. Examples 3-7 (pp. 52-59) disclose the effects of LT-β-R blocking agents in vitro, but for reasons set forth *supra* it is unpredictable whether the results of in vitro experiments are predicably related to (in vivo) methods of treatment. Example 8 (pp. 59-61) discloses that administration of a LT-β-R blocking agent may inhibit a DTH response (ear swelling), but this example is not representative of an immunological disease as defined earlier. Even assuming *arguendo* that the DTH response is a disease, the specification

does not provide evidence of a predictable link between the impairment of a DTH response and treatment methods or therapeutic compositions for any immunological disease. Neither has a link between the methods or compositions and a primary immune response (Example 9) or ex vivo lymphocyte proliferation (Example 10) been established in the disclosure. Thus, the specification provides limited guidance and no working examples wherein an immunologic disease, including diseases in mammals or humans, and further including treatment with a soluble LT-β-R that may selectively bind to a surface LT ligand, and finally including a soluble LT-β-R further comprising a human Fc domain, is treated with a LT-β-R blocking agent. Nor does the specification disclose an example of a pharmaceutical composition comprising a therapeutically effective amount of the LT-β-R agent and a pharmaceutically acceptable carrier, including an example wherein soluble LT-β-R capable of selectively binding to a surface LT ligand.

Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art such as the treatment of immunologic diseases with LT-β-R blocking agents. Further adding to this unpredictability is the fact that different immunological diseases may arise from different defects in the multitude of steps and/or points of entry into an immune-mediated response. In the instant case, the claims are so broadly drawn, and the art is so unsettled that the skilled artisan is presented with a multitude of un-linked and unpredictable alternatives with insufficient guidance as to which will enable use of the invention as claimed. Thus, in view of the lack of guidance in the specification and unpredictability in the art, undue experimentation would be required to enable the method as claimed.

ii. Further regarding claims 2-6, and 39-41, which recite "a soluble lymphotoxin-β receptor", the specification is not enabled for <u>any</u> soluble receptor which binds lymphotoxin-β. Rather, the specification discloses a soluble human lymphotoxin-β receptor comprising SEQ ID NO:1, the extracellular portion of the human lymphotoxin-β receptor, which "binds LT heteromeric complexes but does not bind TNF or LT-α," (p. 18, paragraph 1).

However, for reasons *supra* it is unpredictable whether the soluble receptor alone (i.e., not fused with Fc), is enabled for a method of treatment or pharmaceutical composition.

iii. Further regarding claims 2-4 and 39-41, which recite "surface LT ligand", the specification is not enabled for <u>any</u> surface lymphotoxin ligand. Rather, the specification is enabling for surface ligands comprising lymphotoxin-β, as disclosed at pp. 13-14, bridging paragraph, and/or pp. 14-15, bridging paragraph.

iv. Further regarding claims 5 and 6, the disclosure does not reasonably provide enablement for a soluble LT-β-R, or a soluble LT-β-R further comprising a human Fc domain, that can <u>selectively bind</u> to surface LT ligand. The specification (e.g., pp. 28-29) provides methods that rely on cytotoxic or anti-proliferative effects of soluble LT-β-R to determine which molecules may compete with LT-β-R for binding to surface LT ligand. However, this is not considered to be the same as a competitive binding assay, which would be used to determine binding selectivity, and from which relative affinity or dissociation constants may be determined. In view of the earlier referred to multi-step nature and unsettled art associated with the role of cytokines in the immune response, it is uncertain whether the disclosed competition experiments are predictably linked to the selective binding limitation recited in claim 5. In other words, competitive effects on cytotoxicity or inhibition of cell proliferation may have been due to factors other than competition for a surface ligand binding site. Further, the specification provides limited guidance regarding how the well-known techniques for determining selective binding of immunoglobulins would be applied in a predictable manner to the instant invention. Therefore, in view of the limited guidance in the specification and unpredictability in the art, undue experimentation would be required to enable the invention.

b. Claims 1-6, and 38-41 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 1-6 are indefinite in the recitation of "immunological disease." This is an exceptionally broad term which is not precisely defined in the specification; nor does this term have a precise meaning in the art. Amendment of the claim to recite more specific sub-categories of immunologic diseases, or individual diseases, will overcome this rejection.

Claims 2-6, and 39-41 are indefinite in the recitation of "a soluble lymphotoxin-β receptor." This term is broad and imprecise because it encompasses any non-cell-associated molecule which binds to lymphotoxin-β, including antibodies and other cytokines. Further imprecision arises from the term "receptor," which may refer to any membrane-associated ligand, or in the instant invention, to a specific protein. Assuming applicant intends to refer to the soluble portion of the lymphotoxin-β receptor, phrasing such as --a soluble polypeptide comprising the lymphotoxin-β receptor and capable of binding lymphotoxin-β-- will overcome this rejection.

Claims 2-6, 39, and 40 are indefinite in the recitation of "surface LT ligand." Although the term "LT ligand" is defined on p. 14, paragraph 2, the definition is imprecise in the use of the term "derivative," and therefore the meaning or metes and bounds of "LT ligand" cannot be ascertained. The specification and art of record disclose numerous cytokines or combinations of cytokines which bind to lymphotoxin and therefore may be considered LT ligands.

Applicant is reminded that any amendments must be supported by the specification so as not to add any new matter.

23. Rejections under 35 U.S.C. § 103

a. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to

a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

b. Claims 1-6 and 38-41 are rejected under 35 U.S.C. § 103 as being unpatentable over Crowe et al. (1994; of record) in view of Warzocha et al. (1994).

The claims are drawn to a method of treating or reducing the advancement, severity or effects of immunologic disease by administering a pharmaceutical composition comprising a lymphotoxin-β receptor blocking agent, including such blocking agents as soluble lymphotoxin-β receptor, a lymphotoxin-β receptor that can selectively bind surface lymphotoxin, and a lymphotoxin-β receptor further comprising a human Fc domain. The claims are further drawn to the pharmaceutical composition used in the method *supra*.

Crowe et al. (1994) discloses the lymphotoxin-β receptor, which has a structure homologous with TNF and LT-α receptors (p. 708, column 1, last paragraph, to column 3, last paragraph). The reference further teaches a lymphotoxin-β receptor-Fc chimeric protein which precipitates LT-α-LT-β complexes (a surface ligand), and soluble lymphotoxin-β (p. 708, column 1, paragraphs 1 and 2). Thus, the reference teaches two lymphotoxin-β blocking agents. The reference does not teach a pharmaceutically acceptable carrier.

Warzocha et al. (1994) teaches that soluble TNF/LT receptors may be beneficial in diseases where an imbalance between cytokines and anticytokines can be demonstrated (p. 88, column 1, paragraph 2). The reference further teaches that soluble TNF/LT receptors may inhibit

TNF/LT activity in vivo. Thus, the reference teaches therapeutic use of soluble TNF/LT receptors for the treatment of immunologic disease. The reference does not teach a pharmaceutically acceptable carrier.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the disclosure of Crowe et al. (1994) regarding lymphotoxin-β blocking agents with that of Warzocha et al. (1994) regarding in vivo applications to produce a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a lymphotoxin-β blocking agent, including such blocking agents as soluble lymphotoxin-β receptor, a lymphotoxin-β receptor that can selectively bind surface lymphotoxin, and a lymphotoxin-β receptor further comprising a human Fc domain, and to use that composition in a method of treating immunologic disease. Although not explicitly taught by the references, one of ordinary skill would be expected to construct the composition in any well-known carrier, such as physiologic saline solution, in order to render the composition acceptable for pharmaceutical uses. Alternatively, it would have been obvious to place lymphotoxin-β receptor in any number of pharmaceutically acceptable carriers such as phosphate-buffered saline for use in ligand-receptor assays, or during purification and storage, or for affinity purification of lymphotoxin-β. One would have had a reasonable expectation of success in obtaining the composition in view of the fact that the active ingredients were known to be soluble in physiologic fluids such as plasma. One would have had a reasonable expectation of success regarding the method of treating or reducing the advancement, severity or effects of an immunological disease in view of the teachings of Warzocha et al. (1994) regarding the ability of soluble cytokine receptors, including lymphotoxin-β receptor to attenuate the effects of cytokines such as lymphotoxin-β, and thereby

interfere with an immune-mediated response such as inflammation. Thus, the claimed subject matter is considered to be *prima facie* obvious over the teachings of the prior art, absent sufficient objective factual evidence to the contrary.

24. Examination of the prior art

The following art, extant at the time the invention was made, is relevant to the instant disclosure:

The concept of using soluble forms of cytokine receptors to neutralize the biologic activity of a tumor necrosis factor [Higuchi and Aggarwal (1992); Gatanga et al. (1990)].

A method of making and using a chimeric protein comprising a cytokine and Fc region [Peppel et al. (1991)].

An antibody capable of neutralizing the in vitro activity of lymphotoxin-α [U.S. Patent 4,959,457].

25. No claim is allowed.

26. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray F. Ebert, Ph.D., whose telephone number is (703) 305-7023. The examiner normally can be reached Monday through Friday from 8:30 a.m. to 5:00 p.m., Eastern Standard Time.

Papers related to this application may be submitted to Group 1806 by facsimile

transmission. Submissions by telefax must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The telefax number for this Group is (703) 308-4242.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

RFE

Ray F. Ebert, Ph.D.

Assistant Examiner

PHILLIP GAMBEL
PATENT EXAMINER
GROUP 1500

8505606C.FA

UNITED STAT DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
BANSAL, S	
ART UNIT	PAPER NUMBER
1642	6

KERRY A FLYNN ESQ
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BIOGEN, INC. - IP DEPT.
OCT 04 2000
REFERRED TO NDC
NOTED BY ph

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

ENTERED AR

REMINDER 090C2000
ACTION DUE 01NO2000
END OF STAT 01AP2000

Application No.	Applicant(s)
09/304,267	
Examiner	Group Art Unit

Office Action Summary

---The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address---

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 0 (30 days) MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 4/30/99, 7/24/00.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-67 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-67 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved. ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-14, 38-49, drawn to a method of treating immunological diseases by administering a LT-β-R blocking agent, and to compositions comprising LT-β-R blocking agent, classified in class 424, subclass 85.1, 103.1 and 520, and class 514, subclass 2.

Claims 15-37, drawn to an in vivo method of inhibiting Th1 cell-mediated immunity by administering a LT-β-R blocking agent, classified in class 424, subclass 44.

III. Claims 50-53, drawn to a method for selecting an LT-βR blocking agent, classified in class 435, subclass4, 7.21, 69.1.

IV. Claims 54-67, drawn to an in vivo method for inhibiting signalling through LT-βR, classified in class 514, subclass 2.

V. Claim 50, drawn to a method for detecting C antigen, classified in class 435, subclass 7.23.

2. The inventions are distinct, each from the other because of the following reasons: Inventions I, II, III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MEP. § 806.04, MEP. § 808.01). In the instant case the different inventions are drawn to different methods which are distinct and independent as they require different method steps, reagents, therapeutic variables and rely on different endpoints.

3. Invention drawn to composition of Group I and methods of Groups II and IV are related as product and processes of use. The inventions can be shown to be distinct if either or both of

the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MEP. § 806.05(h)). In the instant case the product of Group I can be also used in immunoaffinity purification methods as well as the different methods of the invention as claimed.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, their recognized divergent subject matter, and the search required for the different Groups are different, restriction for examination purposes as indicated is proper.

5. This application contains claims directed to the following patentably distinct species of the claimed invention, lymphotoxin β-Receptor (LT-β-R) blocking agent:

A. Soluble LT-β-R,

B. Antibody to LT-β-R, or

C. Antibody to surface LT ligand.

These species are are considered patentably distinct because they are structurally different protein. If any of the set forth GroupsI-IV are elected, Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (from A-C) for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 1, 15, 38, 54 are generic.

6. The invention of Group II further recites the following species of diseases:

D. Multiple sclerosis,

E. Insulin dependent diabetes,

F. Sympathetic ophtalmia

G. Uveitis

H. Psoriasis

These species are are considered patentably distinct because they are diseases having different etiologies and therapeutic endpoints which necessitate different searches and raise different enablement issues. If Group II is elected, Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (D-H) for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 15 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently

named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

9. **Please Note**: In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

10. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-3014.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Geetha P. Bansal whose telephone number is (703) 305-3955. The examiner can normally be reached on Mondays to Thursdays from 7:00am to 4:30pm and alternate Fridays from 7:00am to 3:30pm. A message may be left on the examiner's voice mail service.

12. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Anthony Caputa, can be reached on (703) 308-3995.

13. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

September 18, 1999.

GEETHA P. BANSAL
PRIMARY EXAMINER